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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,554	10/03/2003	Qun-Yong Zhou	UC11250-1	9876

28213 7590 12/15/2006

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	**Application No.** 10/680,554	**Applicant(s)** ZHOU ET AL.	
	Examiner Daniel C. Gamett, PhD	**Art Unit** 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-25 and 28-35* is/are rejected.

7)☒ Claim(s) *26 and 27* is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date *08/07/2006 01/26/2005*.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of claims 23-35 in the reply filed on 09/29/2006 is acknowledged. The traversal is on the ground(s) that a thorough search of the claims for either group would reveal art relevant to both Groups. This is not found persuasive for the following reasons. First, the two Groups recite distinct inventions that would support separate patents. Furthermore, a serious burden on the examiner may be *prima facie* shown by appropriate explanation of separate classification, or separate status in the art, or a different field of search (M.P.E.P. 803, II). Separate classification and separate status in the art were established in the restriction requirement. In this case, the prior art searches for each invention center on different sequences and other aspects of patentability, such as enablement, are intrinsically different for a discovery method (Group I) compared to a method of modulating cell differentiation (Group II).

The requirement is still deemed proper and is therefore made FINAL.

2. Upon further consideration, the requirement for election of species is hereby withdrawn.

3. Claims 23-35 are under consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 23-25, and 28-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of stimulating neurogenesis comprising contacting neural stem or progenitor cells with prokineticin peptide agonists selected from the group consisting of SEQ ID NOS: 5-15, does not reasonably provide enablement for methods comprising administration of all potential agonists of any chemical class, nor for methods comprising administration of any PKR antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. The courts have interpreted the first paragraph of 35 U.S.C. 112 to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of

experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

a. *The nature of the invention:* Claim 23 is drawn to a method for modulating neurogenesis, comprising contacting a neural stem or progenitor cell with an effective amount of a compound that modulates prokineticin receptor (PKR) signaling. In dependent claims 24 and 28, the compound that modulates PKR signaling is a PKR agonist and a PKR antagonist, respectively.

b. *The state of the prior art and the predictability or lack thereof in the art:* The prior art is silent regarding PKR agonists that are not prokineticin peptides. The prior art is silent on a role for PKR signaling in neurogenesis. A post filing publication indicates that a PKR antagonist can inhibit PK2-stimulated migration of neuronal progenitors (Ng *et al.*, Science 24 June 2005: Vol. 308. no. 5730, pp. 1923 – 1927; see p.1924, left column). This observation does not support the prediction that a PKR antagonist, by itself, would have any effect on neurogenesis, as indicated by the claim.

c. *The amount of direction or guidance present and the presence or absence of working examples:* Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification provides Example V, wherein a PKR agonist, human PK2, was administered to rats and proliferation of cells in neurogenic regions of the brain was observed. The specification provides no example of any effect of a PKR antagonist in any model system.

d. *The breadth of the claims and the quantity of experimentation needed:* A skilled artisan could test the small genus of known prokineticin proteins for agonist activity similar to that shown for PK2 in Example V without undue experimentation. It is not known whether any amount of experimentation will enable PKR agonists that are not prokineticin peptides, or whether a PKR antagonist will have an effect on neurogenesis.

7. Claims 23, 24, and 28-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 23 is drawn to a method for modulating neurogenesis, comprising contacting a neural stem or progenitor cell with an effective amount of a compound that modulates prokineticin receptor (PKR) signaling. In dependent claims 24 and 28, the compound that modulates PKR signaling is a PKR agonist and a PKR antagonist, respectively. The fact that a patent is directed to method entailing use of a compound, rather than to the compound *per se*, does not remove patentee's obligation to provide description of the compound sufficient to distinguish infringing methods from noninfringing methods (University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004)). In this case, the claims are drawn to methods that comprise administration of genera of compounds recited as “a compound that modulates prokineticin receptor (PKR) signaling”, “PKR agonist” and “PKR antagonist”. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any

combination thereof. In this case, the claimed compounds are described only by function, without any structural limitation. In claim 23, the function is broadly defined; the compound need not interact with PKR or prokineticin, but could target any component of a pathway regulated by PKR to bring about any kind of change in the signal. The specification only discloses that prokineticin peptides selected from the group consisting of SEQ ID NOS: 5-15 are PKR agonists. The specification teaches that PKR antagonists may be created by N-terminal modification of prokineticin peptides ([0056] of the published specification). These examples are not sufficient to provide written description of all molecules of all chemical classes that may share similar functions.

8. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

9. With the exceptions of SEQ ID NOS: 5-15, and certain N-terminal deletions and additions known in the art, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v.*

Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

10. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

11. Therefore, only methods comprising contacting cells with peptides comprising the amino acid sequences set forth in SEQ ID NOS: 5-15, or PKR antagonists known in the art, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 35 recites the limitation "said human cell" in claim 33. There is insufficient antecedent basis for this limitation in the claim; the cell recited in claim 33 is mammalian, but not necessarily human. Applicant apparently intended that claim 35 should depend from claim 34.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 23-25, 32, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Mollay *et al.*, Eur J Pharmacol. 1999 Jun 18;374(2):189-96 (citation no. 31, IDS filed 01/26/2005). Mollay et al. injected Bv8 isolated from *Bombina variegata* and Protein A from black mamba (*Dendroaspis polylepis*) into rat brain ventricles (see sections 2.2 and 2.6). This procedure necessarily brings the injected proteins into contact with neural stem and progenitor cells. The instant specification stipulates that Bv8 from *Bombina variegata* and Protein A from black mamba are prokineticin peptides comprising the amino acid sequence of SEQ ID NOS: 13 and 12, respectively. Thus Malloy *et al.*, performed all of the recited method steps by contacting mammalian neural stem or progenitor cells *in vivo* with a PKR agonist selected from the group consisting of SEQ ID NOS: 5-15. Contacting neural progenitor cells with Bv8 or Protein A would necessarily bring about all of the responses inherent to Bv8 or Protein A, including stimulating neurogenesis.

Conclusion

16. Claims 23-25, and 28-35 are rejected.

17. Claims 26 and 27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D.,whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647
11 December 2006

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